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(54) Test strip for determining dialysate composition

(57) A test strip (10) for confirming a desired proportion of components in dialysate, including a first medium capable of indicating the concentration of bicarbonate ion, and a second medium capable of indicating the concentration of glucose. The test strip (10) defines a first region (11) impregnated with the first medium, and a second region (12) impregnated with the second medium. The test strip optionally includes a third medium capable of indicating the pH of the dialysate. The third medium is impregnated at a third region (13) on the test strip. Alternatively, the test strip (15) comprises a bicarbonate test pad attached to a first region (16), a glucose test pad attached to a second region (17), and optionally a pH test pad attached to a third region (18). The glucose test pad is impregnated with the first medium, the glucose test pad is impregnated with the second medium, and the pH test pad is impregnated with the third medium.

EP 1 211 512 A2

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Description

Field of the Invention.

[0001] The present invention relates to the testing of dialysates, used in kidney dialysis, to confirm that the dialysates are safe for use to cleanse the blood of patients with kidney failure. More particularly, the present invention relates to devices and methods for confirming that the components of dialysates are present in the correct proportions.

Description of the Related Art.

[0002] Dialysates are used in kidney dialysis (hemodialysis) to cleanse the blood of patients with kidney failure. Generally, dialysate is a solution of buffered salts and glucose in purified water. In the majority of dialysates, a bicarbonate ion is the buffering ion. Bicarbonate dialysate is prepared by combining a bicarbonate concentrate with an acid concentrate, and then diluting the mixture with purified water to obtain the correct proportion of the dialysate components. Clinical technicians may prepare the bicarbonate concentrate "on site" at a dialysis facility, but more commonly, the bicarbonate concentrate is purchased along with the acid concentrate from a commercial supplier.

[0003] The dialysate is typically prepared by a dialysis machine, which performs the actual combining, mixing and diluting of the bicarbonate and acid concentrates. Dialysis machines generally include a blood pump, a dialysis solution delivery system, and appropriate safety monitors. There are two major types of dialysis solution delivery systems, a central proportioning delivery system and an individual proportioning system. In the central proportioning delivery system, all of the dialysate is produced by a single machine, and the dialysate is then pumped through pipes to individual dialysis machines. In an individual proportioning delivery system, each dialysis machine proportions the dialysate separately. The blood pump moves the patient's blood to a dialyzer where the blood is cleansed with the dialysate. The cleansed blood is returned to the patient, and the used dialysate flows into a drain and is discarded.

[0004] If the proportioning system that dilutes the bicarbonate and acid concentrates with water malfunctions, an excessively dilute or concentrated dialysate may be produced. Daugirdas, J.T., Ing, T.S., Handbook of Dialysis, 2nd ed., Little, Brown and Company, Boston/New York/Toronto/London, 1994, p.48. Exposure of blood to a severely hyperosmolar (too concentrated) dialysate can lead to hypernatremia and other electrolyte disturbances, while exposure to a severely hypoosmolar (too dilute) dialysate can result in rapid hemolysis or hyponatremia. Id. It is therefore critical to ensure that the dialysate is proportioned correctly such that it is safe for use with the blood of a patient before dialysis begins. According to the industry standards, the pH of dialysate should be between 6.0 and 8.0. ANSI/AAMI RD5, § 3.3.1.6 (1992). Additionally, all solutes identified on a concentrate label should be present within +/- 5% of the stated concentration or weight, while sodium and chloride, in particular, should be present within +/- 2% of the labeled concentration or weight. ANSI/AAMI RD5, § 3.3.1.2 (1992). Generally, the concentration of the ionic components of the dialysate can be indirectly determined by the electrical conductivity of the dialysate, because the primary solutes in dialysates are electrolytes.

[0005] Most dialysis machines are equipped with built-in meters or other safety devices that continuously monitor, among other variables, dialysate concentration and pH. The pH of the dialysate is typically measured by means of a glass pH electrode built into the dialysis system. The dialysate concentration is typically determined indirectly by measuring the electrical conductivity of the dialysate with a conductivity meter.

[0006] One problem with these safety devices is that both the conductivity meters and the glass pH electrodes require routine maintenance and calibration checks to insure proper operation. Disadvantageously, this maintenance and calibration checks are time consuming, and are often beyond the technical capability of clinic personnel.

[0007] Further disadvantages result from the nature of the conductivity and pH measurements. Specifically, because conductivity is a measurement of the total ion concentration in solution, it is therefore a nonspecific measurement of the concentrations of particular ionic components in the dialysate. This nonspecific measurement can fail because both the bicarbonate concentrate and acid concentrate each contain specific ionic components. In some cases, the observed conductivity measurements are correct, when in fact, the proportion of the bicarbonate and acid concentrates is incorrect. For example, if the concentration of one of the concentrates is too high and the other is too low, the concentrate whose concentration is too high will compensate for the concentrate whose concentration is too low. This results in a conductivity measurement that is mistakenly observed as an indication that the dialysate composition is correct. This problem is recognized in the above-referenced ANSI/AAMI standard, which states:

[0008] *Adequate monitoring does not currently exist to assure that mismatched concentrates will not produce a final dialysate of proper total conductivity but improper composition. The user is cautioned not to rely solely on conductivity measurements to ensure safety, but to consider all relevant factors, including pH.*

[0009] ANSI/AAMI RD5, § 3.3.1.6 (1992) (emphasis in original). Another concern with the current systems is that pH measurements are also by nature, as logarithmic measurements, insensitive to errors in the proportion of the bicarbonate and acid concentrates in the dialysate. Only substantial changes in the proportion of the bicarbonate and

[0022] Another advantage of the tests of this invention is that they are easy to use and to interpret.

[0023] Still another advantage of this invention is that it allows a user who does not possess advanced scientific and/or technical training to obtain a quick and reliable visual confirmation of whether the bicarbonate and acid concentrates are present in the correct proportion in dialysate.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] The above mentioned and other features and objects of this invention, and the manner of attaining them, will become more apparent and the invention itself will be better understood by reference to the following description of an embodiment of the invention taken in conjunction with the accompanying figures, wherein:

[0025] Figure 1 is a front elevational view of a test strip in accordance with one embodiment of the present invention;

[0026] Figure 2 is a side elevational view of the test strip of Figure 1;

[0027] Figure 3 is a front elevational view of another test strip in accordance with another embodiment of the present invention; and

[0028] Figure 4 is a side elevational view of the test strip of Figure 3.

[0029] Although the drawings represent embodiments of the present invention, the drawings are not necessarily to scale and certain features may be exaggerated in order to better illustrate and explain the present invention. The exemplification set out herein illustrates an embodiment of the invention, in one form, and such exemplifications are not to be construed as limiting the scope of the invention in any manner.

DETAILED DESCRIPTION

[0030] The embodiments disclosed below are not intended to be exhaustive or limit the invention to the precise forms disclosed in the following detailed description. Rather, the embodiments are chosen and described so that others skilled in the art may utilize their teachings.

[0031] The present invention provides an apparatus and method for checking dialysate makeup by measuring at least one ingredient from each of the bicarbonate concentrate and acid concentrate of the dialysate. If both are in the correct range, then the proportions of all three components, namely, the bicarbonate concentrate, the acid concentrate, and water must be in the acceptable range. The bicarbonate ion is derived only from the bicarbonate concentrate and thus can be used as the marker for bicarbonate concentrate. Of the number of ingredients unique to the acid concentrate, glucose is the most suitable marker because it is present at a consistent level in almost all dialysates.

[0032] In accordance with the present invention as shown in Figures 1-4, the test strip for confirming the desired proportion of bicarbonate and acid concentrates in dialysate comprises a first medium capable of indicating the concentration of bicarbonate ion, and a second medium capable of indicating the concentration of glucose in the dialysate. Further, the test strip optionally comprises a third medium capable of indicating the pH of the dialysate. The test strip can be made of any suitable bibulous carriers, such as filter paper, or sponges. Additionally, other materials such as beaded columns or wooden sticks are contemplated.

[0033] In an exemplary embodiment shown in Figures 1-2, test strip **10** includes a first medium impregnated thereon at a first region **11**, and a second medium impregnated thereon at a second region **12**. Test strip **10** optionally includes a third medium impregnated thereon at a third region **13**. The third medium is capable of indicating the pH of the dialysate. The pH determination is used as an additional test to confirm whether the concentrates are in the right proportion. It is not critical how the regions are arranged on the test strip.

[0034] In another embodiment shown in Figures 3-4, test strip **15** includes a bicarbonate test pad localized at a first region **16**, a glucose test pad localized at a second region **17**, and optionally, a pH test pad localized at a third region **18**. Each region may be disposed in any order from an end of test strip **15**. The bicarbonate test pad is impregnated with the first medium capable of indicating bicarbonate ion concentration, the glucose test pad is impregnated with the second medium capable of indicating glucose concentration, and the pH test pad is impregnated with the third medium capable of indicating the pH of the dialysate. Exemplarily, the test strip **15** includes a backing material **19**. The backing material can be made of any suitable materials, such as plastic, poly-styrene, paper, wood, or glass.

[0035] In the exemplary embodiments, each medium is prepared following the concepts and procedures described herein below.

Bicarbonate Concentration

[0036] The concentration of bicarbonate ion in a dialysate sample is determined by measuring the buffering capacity of the bicarbonate concentrate on a bicarbonate test pad impregnated with the first medium. The first medium includes an acid and a chromogenic pH indicator. During the bicarbonate measurement, the acid in the test pad reacts with the bicarbonate in the dialysate sample. The chemical reaction ultimately alters the pH of the pH indicator within the test

pad. The pH indicator is a substance capable of exhibiting a color change responsive to pH changes. The final color of the indicator is matched with a corresponding color on a standard color chart that shows the corresponding pH value. The higher the pH value indicates the higher concentration of the bicarbonate in the dialysate sample. For example, when sodium bicarbonate is present in the dialysate sample, the following reaction (I) occurs within the bicarbonate test pad:

$$(I)\quad NaHC0_3 + 2R^-H^+ \longrightarrow H_2C0_3 + R^-H^+ + R^-Na^+$$

(Sodium bicarbonate + Acid) (Carbonic Acid) Sodium Salt

[0037] The acid within the bicarbonate test pad reacts with sodium bicarbonate and forms carbonic acid. In addition, a ratio of R^-H^+ / R^-Na^+ is generated in the test pad, at the completion of the reaction. This ratio is determined by the amount of sodium bicarbonate originally present in the test sample. In turn, the R^-H^+ / R^-Na^+ determines the test pad pH, which can be measured by means of a chromogenic pH indicator. The color of the pH indicator changes with its pH.

[0038] Suitable acids that can be used in the bicarbonate test pad are acids having a pKa value of about one unit below that of the bicarbonate ion (pKa = 6.4). Acids having pKa values of more than one unit below or less than one unit below that of the bicarbonate ion can also be used. However, the use of the acids having very low pKa value may not be feasible due to the lack of suitable pH indicators. In addition, since a dry medium is preferred, the acid must be a nonvolatile solid. Also, to allow for short reaction times, the acid should be water-soluble. Examples of suitable acids are listed in TABLE 1. The pKa values of these acids are within the desired range of between 2.9 and 5.6. Lange's Handbook of Chemistry, 14th Ed., McGraw-Hill, Inc., New York (1992). The invention also contemplates any suitable acid.

TABLE 1:

Examples of suitable acids	
Acid	pKa
Citric acid	3.1; 4.7 and 5.4
Succinic acid	4.2 and 5.6
Tartaric acid	2.9 and 4.2
Phthalic acid	3.0 and 5.4
Fumaric acid	3.1 and 4.6
Gluconic acid	3.9

[0039] The chromogenic pH indicator is capable of exhibiting a color change when its pH changes. Suitable pH indicators for a bicarbonate test pad should have a pKa value in the same range as that of suitable acids. An indicator with a pKa value in the same range as that of the bicarbonate ion may also be used, but the results may be less predictable since the buffering capacity will vary with bicarbonate concentration. The pKa values of suitable pH indicators (TABLE 2) range from 3.8 to 7.6. Merck Index, 10th Edition, Merck & Co., Inc. (1983). It is contemplated that other pH indicators having pKa values slightly below or above the above range may also be used.

TABLE 2:

Examples of suitable pH indicators			
Indicator	pKa	Color change	
		Low Bicarbonate ——> High	
Bromophenol blue	3.8	Yellow	Blue
Methyl orange	3.8	Red	Yellow
Tetrabromophenol blue	3.8	Yellow	Blue
Congo red	4.0	Blue	Red

TABLE 2: (continued)

Examples of suitable pH indicators			
Indicator	pKa	Color change	
		Low Bicarbonate ----> High	
Bromocresol green	4.6	Yellow	Blue
Litmus	6.5	Red	Blue
Phenol red	7.6	Yellow	Red

[0040] Generally, the bicarbonate test pad should have a broad range of sensitivity because it is desirable to be able to detect a broad range of bicarbonate concentrations in dialysate samples. Particularly, the test should be sensitive enough to detect the bicarbonate concentration in dialysates made from mixing commercial bicarbonate and acid concentrates. It is contemplated that the test is sensitive enough to determine bicarbonate concentration in dialysates prepared by any dialysis machine. The target or the proper dialysate produced by any of the three main types of dialysis machines: 1/36.83 Proportioning System (Drake, Gambro, Baxter, Althin, Braun), 1/35 Proportioning System (Fresenius), and 1/45 Proportioning System (Cobe Machines) contains bicarbonate ion concentration of about 37 ± 2 mEq/L. Of course, it is not possible to estimate the range of concentrations that might result from errors in the bicarbonate concentrate preparation or machine function. Ideally, the test would be able to detect small dialysate deviations arising from these errors. A possible range of incorrect concentrations derived from using a wrong concentration of bicarbonate concentrate and/or acid concentrate with a wrong machine is calculated in the range of 21.4 to 49.7 mEq/L. Also, the test should clearly indicate the situation in which the bicarbonate is very high (about 1200 to 1655 mEq/L in the concentrate) or is missing entirely.

Glucose Concentration

[0041] The determination of glucose concentration in a dialysate sample is based on reactions (II) and (III) shown below. The first reaction utilizes an enzyme, glucose oxidase (EC 1.1.3.4), to catalyze oxidization of glucose by atmospheric oxygen to form hydrogen peroxide. The second reaction utilizes an enzyme, horseradish peroxidase (EC 1.11.1.7), to catalyze oxidization of a chromogenic oxidation/reduction indicator by hydrogen peroxide.

$$\text{Glucose} + O_2 \xrightarrow{\text{(reaction catalyzed by glucose oxidase)}} \text{Gluconic Acid} + H_2O_2$$

$$H_2O_2 + \text{Reduced Indicator} \xrightarrow{\text{(reaction catalyzed by horseradish peroxidase)}} \text{Oxidized Indicator} + H_2O$$

[0042] The chromogenic oxidation/reduction indicator is a substance which, after being oxidized or reduced by hydrogen peroxide, is capable of forming a color different from its original color. The degree of color change depends on the amount of hydrogen peroxide generated, which, in turn, depends on the amount of starting glucose. Therefore, if glucose is present in the dialysate, the color of the indicator in the glucose test pad will change depending on the concentration of the glucose. The final color of the test pad is matched with a corresponding color on a standard chart to indicate a corresponding concentration of glucose.

[0043] In the exemplary embodiments, the glucose oxidase enzyme is derived from a microbial source such as *Aspergillus niger* or *Penicillium reticulosum*. However, glucose oxidase from other sources may also be applicable as long as it catalyzes the transition of glucose with the concomitant production of hydrogen peroxide.

[0044] Horseradish peroxidase is used in the exemplary embodiments as the catalytic enzyme for the second reaction, however, peroxidase from other sources or any other suitable enzyme is also contemplated.

[0045] Examples of suitable oxidation/reduction indicators are presented in TABLE 3. Conyers, S.M., and Kidwell, D.A., Analyt. Biochem. 192 (1991) or Blake, D.A. and McLean, N.V., Analyt. Biochem 177 (1989). It is contemplated that other substances which exhibit a color change upon reaction with hydrogen peroxide may also be applicable.

TABLE 3:

Examples of suitable oxidation/reduction indicators		
Indicator	Maximum Absorbance (nm)	Color
o-Dianisidine	460	Yellow
4-AAP/phenol	505	Red/Yellow
MBTH/3-dimethylaminobenzoic acid	590	Red
Tetramethyl benzidine	650	Blue
Potassium iodide	352	Yellow/Brown

[0046] It is also possible that the glucose test pad may be treated with an inert dye of a particular color such as yellow or blue, so that the color change exhibited by the oxidation/reduction indicator is blended with the background color to produce varying tints which correspond to different concentrations of glucose present in the dialysate being tested.

[0047] In the exemplary embodiments, the glucose test pad has a broad range of sensitivity. Generally, the glucose test pad would be able to detect the glucose concentration in various dialysate samples. Particularly, the test pad should detect the glucose concentration in dialysates made from commercial concentrates or by dialysis machines. The target dialysate produced by any of the three main types of dialysis machines: 1/36.83 Proportioning System (Drake, Gambro, Baxter, Althin, Braun), 1/35 Proportioning System (Fresenius), and 1/45 Proportioning System (Cobe Machines) contains a glucose concentration of 2 g/L. Of course, it is not possible to estimate the range of concentrations that might result from errors in machine function. Ideally, the test would be able to detect small dialysate deviations arising from these errors. A possible range of incorrect concentrations derived from using a wrong concentration of bicarbonate concentrate and/or acid concentrate with a wrong machine is in the range of 1.55 to 2.57 g/L. Also, it should clearly indicate instances where glucose is well above normal (about 70 to 90 g/L) in the concentrate or is missing entirely.

pH

[0048] The acceptable pH range for the dialysates is 6.0 to 8.0 (ANSI/AAMI RD5-1992, paragraph 3.3.1.6.). The pH of dialysates may be determined by means of a standard pH indicator. However, ideally, the pKa of the pH indicator should be about 7.0. In the exemplary embodiments, the test for pH of dialysates makes use of the Serim Bicarb pH Test Strip (Serim Research Corp., Elkhart, IN), which has the applicable sensitivity range. Examples of suitable pH indicators (Merck Index, 10th Edition, Merck & Co., Inc. (1983), pp. MISC. 104-105) are listed below in TABLE 4.

TABLE 4:

Examples of suitable pH indicators		
Indicator	pKa	Color Change
		Low pH ——> High pH
Bromothymol blue	6.8	Yellow ——> Blue
Pyrocatechol violet	7.0	Yellow ——> Violet
Tetra-bromophenol sulfonephthalein	7.4	Yellow ——> Purple
Neutral red	7.4	Red ——> Yellow
Phenol red	7.6	Yellow ——> Red
Cresol red	7.9	Yellow/red ——> Purple

EXAMPLE 1

Preparation of the bicarbonate test pad

[0049] The first medium containing at least one acid, at least one pH indicator, and water is prepared as one of the formulations listed herein below. The first medium may include salts and other inert reagents. It is to be understood that these formulations have been chosen as illustrative of the present invention and it will, of course, be apparent to those skilled in the art that various modifications may be made without departing from the spirit and the scope of the present invention.

Formulation 1	
Ingredient	Amount
Citric Acid	0.02 g [0.000706 oz]
Sodium Citrate	0.035 g [0.001236 oz]
Nitrazine Yellow	0.01 g (Inert background colorant) [0.000353 oz]
Bromocresol Green	0.02 g [0.000706 oz]
Water	100 mL [3.5195 fl. oz]

[0050] Hydrochloric acid was added to the above mixture until the pH, as monitored with a glass pH electrode, reached a value of 2.6.

Formulation 2 (Varying the Acid Content of the Test Pad)	
Ingredient	Amount
Citric Acid	0.04 g [0.001412 oz]
Sodium Citrate	0.07 g [0.002471 oz]
Nitrazine Yellow	0.01 g (Inert background colorant) [0.000353 oz]
Bromocresol Green	0.02 g [0.000706 oz]
Water	100 mL [3.5195 fl. oz]

[0051] Hydrochloric acid was added to the above mixture until the pH, as monitored with a glass pH electrode, reached a value of 2.6.

Formulation 3 (Varying the Acid Content of the Test Pad)	
Ingredient	Amount
Citric Acid	0.08 g [0.002824 oz]
Sodium Citrate	0.14 g [0.004942 oz]
Nitrazine Yellow	0.01 g (Inert background colorant) [0.000353 oz]
Bromocresol Green	0.02 g [0.000706 oz]
Water	100 mL [3.5195 fl. oz]

[0052] Hydrochloric acid was added to the above mixture until the pH, as monitored with a glass pH electrode, reached a value of 2.6.

Formulation 4 (Varying the Acid Content of the Test Pad)	
Ingredient	Amount
Citric Acid	0.30 g [0.01059 oz]
Sodium Citrate	None
Nitrazine Yellow	0.01 g (Inert background colorant) [0.000353 oz]
Bromocresol Green	0.02 g [0.000706 oz]
Water	100 mL [3.5195 fl. oz]

[0053] Hydrochloric acid was added to the above mixture until the pH, as monitored with a glass pH electrode, reached a value of 2.6.

Formulation 5 (Varying the Acid Content of the Test Pad)	
Ingredient	Amount
Citric Acid	0.45 g [0.015885 oz]
Sodium Citrate	None
Nitrazine Yellow	0.01 g (Inert background colorant) [0.000353 oz]
Bromocresol Green	0.02 g [0.000706 oz]
Water	100 mL [3.5195 fl. oz]

[0054] Hydrochloric acid was added to the above mixture until the pH, as monitored with a glass pH electrode, reached a value of 2.6.

Formulation 6 (Varying the Indicator and the pH of the Formula)	
Ingredient	Amount
Citric Acid	0.08 g [0.002824 oz]
Sodium Citrate	0.14 g [0.004942 oz]
Cresol Red	0.02 g [0.000706 oz]
Water	100 mL [3.5195 fl. oz]

[0055] Hydrochloric acid was added to the above mixture until the pH, as monitored with a glass pH electrode, reached a value of 6.0.

Formulation 7 (Varying the Indicator and the pH of the Formula)	
Ingredient	Amount
Citric Acid	0.08 g [0.002824 oz]
Sodium Citrate	0.14 g [0.004942 oz]
Phenol Red	0.02 g [0.000706 oz]
Water	100 mL [3.5195 fl. oz]

[0056] Hydrochloric acid was added to the above mixture until the pH, as monitored with a glass pH electrode, reached a value of 6.0.

[0057] Pieces of filter paper were saturated with the first medium and then dried in a forced-air oven at 60°C for 10 minutes. The dried pads were then used to prepare test strips. The test strips consist of a 3.25 x 0.2 inch [8.255 x 0.5080 cm] strip of backing material such as polystyrene, and a 0.2 x 0.2 inch [0.5080 x 0.5080 cm] bicarbonate test pad attached at one end by means of double-sided adhesive tape.

Test of bicarbonate test pad

[0058] In order to determine the effectiveness of the test pads made with different formulations, the test strips were dipped in the individual dialysate samples containing 0.5X, 1X and 2X concentrations of bicarbonate, where X = 37 ± 2 mEq/L. After two seconds, the strips were removed from the dialysates. The color of each test pad was allowed to develop for about one minute. The results in Table 5 show that the color of the test pads made with Formulations 1-5 changes from yellow to green to blue with the increased bicarbonate concentration. Formulation 5 gives the best color spread and allows the detection of small deviations of bicarbonate concentration. Formulations 1-4 also give similar results. The test pads made from Formulations 6 and 7 exhibited color changes from yellow to orange or red with the increased bicarbonate concentration, and also give good color spreads.

TABLE 5:

Result of the testing of bicarbonate test pads		
Bicarbonate test pad	Bicarbonate concentration	Pad color
Formulation 1-5	0.5X	Yellow
	1X	Green
	2X	Blue
Formulation 6-7	0.5X	Yellow
	1X	Orange
	2X	Red

EXAMPLE 2

Preparation of a glucose test pad

[0059] [00121] The second medium contains glucose oxidase, peroxidase, a chromogenic oxidation/reduction indicator, and water. In addition, acids, salts, and inert ingredients may be added. The second medium can be prepared by following Formulation 8:

Formulation 8	
Ingredient	Amount
Citric Acid	0.38 g [0.013414 oz]
FD&C Blue [0.000706 oz]	0.02 g (Inert background color) [0.000706 oz]
Sodium Citrate	5.29 g [0.1867 oz]
Polyvinyl pyrrolidone	0.50 g [0.01765 oz]
Potassium iodide	1.00 g [0.0353 oz]
Glucose oxidase	0.30 g [0.0159 oz]
Peroxidase	0.70 g [0.02471 oz]
Water	100 mL [3.5195 fl. oz]

[0060] It is to be understood that the aforementioned formulation has been chosen as illustrative of the present invention and it will, of course, be apparent to those skilled in the art that various modifications may be made without departing from the spirit and the scope of the present invention. For example, other suitable oxidation/reduction indicators as listed in TABLE 3 may be used in place of potassium iodide.

[0061] To prepare the glucose test pad, pieces of filter paper were saturated with the solution of formulation 8 and then dried in a forced-air oven at 55°C for 10 minutes. The dried pads were then used to prepare test strips. The test strips included a 3.25 x 0.2 inch [8.255 x 0.5080 cm] polystyrene strip as a backing material, and a 0.2 x 0.2 inch [0.5080 x 0.5080 cm] glucose test pad was attached at one end by means of double-sided adhesive tape.

Test of glucose test pad

[0062] To determine the effectiveness of the glucose test pad in measuring glucose concentration in dialysate samples, the glucose test strip was dipped into the dialysate samples containing 1.0 and 2.0 g/L glucose for one second. The strip was then removed from the samples and the change in color of the glucose test pad was observed. The color of the pad changed from the original shade of yellow/brown to a fully developed color of a different shade in about two minutes. The results shown in TABLE 6 indicate that a glucose concentration between 1.0 and 2.0 g/L in dialysate samples is readily distinguishable. The 1.0 and 2.0 g/L glucose concentration is representative of a low glucose concentration, whereas 2.0 g/L is the expected glucose concentration in standard dialysates.

TABLE 6:

Result of the test of glucose test pad	
Glucose Concentration (g/L)	Final Color of Glucose Test Pad
1.0 (low concentration)	Blue/Green
2.0 (standard Concentration)	Green

EXAMPLE 3

Preparation of test strips having multiple test pads.

[0063] The first medium is prepared as Solution 1, the second medium is prepared as Solution 2, and the third medium is prepared as Solution 3 as listed below. Pieces of filter paper were respectively saturated with each of the three Solutions 1-3 and then dried for 15 minutes in a forced-air oven at 60°C. The dried papers were processed to yield 0.2 x 0.2 inch [0.5080 x 0.5080 cm] pads. Two or three pads, one made with each solution, were attached to one end of a 0.2 x 3.25 inch [8.255 x 0.5080 cm] strip of backing material by means of double-sided adhesive tape.

Solution 1. (bicarbonate test)	
Ingredient	Amount
Citric acid	0.08 g [0.02824 oz]
Sodium citrate	0.14 g [0.004942 oz]
Nitrazine yellow	0.01 g [0.000353 oz]
Bromocresol green	0.02 g [0.000766 oz]
Water	100 mL [3.5195 fl. oz]
pH adjusted to 2.6	

Solution 2. (glucose test)	
Citric acid	0.19 g [0.006707 oz]
FD&C blue	0.01 g [0.000353 oz]
Sodium citrate	2.645 g [0.09337 oz]
Polyvinyl pyrrolidone	0.25 g [0.009178 oz]
Potassium iodide	0.50 g [0.01765 oz]
Glucose oxidase	0.1975 g [0.0066972 oz]
Peroxidase	0.3718 g [0.013125 oz]
Water	50 mL [1.7598 fl. oz]

Solution 3. (pH test)	
m-cresol purple	0.072 g [0.002542 oz]
3,4,5,6-TBPS	0.09 g [0.003177 oz]
Water	50 mL [1.7598 fl. oz]
Reagent alcohol	50 mL [1.7598 fl. oz]
pH adjusted to 7.5	

[0064] It is to be understood that the above solutions have been chosen as illustrative of the present invention and it will of course be apparent to those skilled in the art that various modifications may be made without departing from the spirit and the scope of the present invention. For example, Solution 1 may be made by replacing bromocresol green with any of the pH indicators listed in TABLE 4. Solution 2 may contain, instead of potassium iodide, any of the suitable color indicators listed in TABLE 3. Solution 3 may be replaced by any of the formulations listed in EXAMPLE 1.

Determination of dialysate compositions using a three-test strip.

[0065] In order to test whether the three-test strip prepared as described above is effective in determining glucose concentration, bicarbonate concentration, and pH of dialysates, dialysate samples were prepared by mixing known amounts of commercially available acid and bicarbonate concentrates. Five sets of samples designated "low glucose-low bicarbonate", "target", "high glucose-high bicarbonate", "low glucose-high bicarbonate", and "high glucose-low carbonate" were prepared (TABLE 7). The term "low" in the above designations indicates that only half of the correct amount of the concentrate was present, and the term "high" indicates that twice the correct amount of the concentrate was present. The term "target" indicates that the correct amounts of both acid and bicarbonate concentrates were present, wherein the concentration of bicarbonate is 37 ± 2 mEq/L, and the concentration of glucose is 2.0 g/L. The three-test strips were prepared according to EXAMPLES 1 and 2, and were dipped into the dialysate samples for one second. At 10 seconds after removing the strip from the sample, the color of the pH pad was compared to a standard color chart (Serim. Bicarb pH Test Strips Chart, Serim Research Corp., Elkhart, IN). At 15 seconds, the color of the glucose pad is compared to a corresponding color chart (The Screen Tint Selector, published by Moosberg and Company, 301 East Sample Street, South Bend, IN 46624), and at 30 seconds, the color of the bicarbonate pad is compared to a corresponding color chart. (The Screen Tint Selector, published by Moosberg and Company, 301 East Sample Street, South Bend, IN 46624). It should be noted that the reading time may vary depending on the composition of the solutions used to make the individual test pads.

[0066] The results summarized in TABLE 7 show that the three-test strips are effective in detecting different compositions of bicarbonate and acid concentrates in the dialysate samples. The final colors of the three test pads on each test strip indicate the bicarbonate concentration, the pH of the solution, and the glucose concentration. As expected, the solution having a "target" composition shows the bicarbonate concentration to be at target and the glucose concentration at 2.0 g/L, with the pH of the solution at 7.0. The pH of the "target" solution, as determined by the pH pad, confirms the correct composition of the bicarbonate and acid concentrates.

[0067] The dialysate with low acid concentrate and low bicarbonate concentrate shows a low bicarbonate concentration as read by the bicarbonate test pad, a pH of 7.0 as read by the pH test pad, and a low glucose concentration of 1.0 g/L. The dialysate with high acid concentrate and high bicarbonate concentrate shows a high bicarbonate concentration as read by the bicarbonate test pad, a high pH of 7.4 as read by the pH test pad, and a high glucose concentration of 3.5 g/L. The dialysate with low acid concentrate and high bicarbonate concentrate shows a high bicarbonate concentration as read by the bicarbonate test pad, a high pH of 8.5 as read by the pH test pad, and a low glucose concentration of 1.0 g/L. The dialysate with high acid concentrate and low bicarbonate concentrate shows a low bicarbonate concentration as read by the bicarbonate test pad, a low pH of 6.5 as read by the pH test pad, and a high glucose concentration of 3.5 g/L.

[0068] It is to be noted that when both the acid and bicarbonate concentrates are either high or low, the pH value changes very little. However, the glucose and bicarbonate pads clearly indicate a deviation from the correct concentration in all four incorrect solutions.

TABLE 7:

Results of dialysate test using three-test strips			
Concentrate Levels in Dialysates	pH Test Pad Result (pH)	Bicarbonate Test Pad Result	Glucose Test Pad Result (g/L)
Target	7.0	Target (Green)	2.0 (target)
Low acid and Low Bicarbonate	7.0	Low (Yellow)	1.0
High acid and High Bicarbonate	7.4	High (Blue-Green)	3.5
Low acid and High Bicarbonate	8.5	High (Blue-Green)	1.0
High acid and Low Bicarbonate	6.5	Low (Yellow)	3.5

[0069] It should be noted, however, that a test strip may be prepared in accordance with EXAMPLE 2 including only bicarbonate and acid test pads, which test strip would indicate the results set forth in TABLE 7 with respect to the

bicarbonate and acid concentrate levels. Therefore, a test strip including only bicarbonate and acid test pads may be used to determine whether a dialysate sample includes the correct proportions of bicarbonate and acid concentrates. In this regard, the presence of a pH test pad is optional, wherein the pH test pad result serves to confirm the indications provided by the bicarbonate and acid test pads.

[0070] The examples described herein above demonstrate the procedures for making and using test strips for verifying the proportion of bicarbonate and acid concentrates in dialysate. The examples describe several formulations that can be used as the first medium for indicating bicarbonate ion concentration, representing the proportion of the bicarbonate concentrate in the dialysate. The examples further describe a formulation that can be used as the second medium for indicating the concentration of glucose, representing the proportion of the acid concentrate in the dialysate. In accordance with the present invention, there is a possibility of using alternative formulations or ingredients in the production of the test strips. This possibility is advantageous, especially where the availability or the cost of certain ingredient is limiting.

[0071] In addition to the bicarbonate ion and glucose concentration, the test strip, in accordance with the present invention, further includes a third medium capable of indicating the pH of the dialysate. The pH measurement is used as an additional test that confirms whether the proportion of the concentrates in the final dialysate is correct.

[0072] Based on the above examples, it is clear that the test strips and the methods disclosed herein can be used to accurately and reliably confirm the target proportion of the bicarbonate and the acid concentrates. This confirmation is necessary to ensure that the proper composition of the dialysate is being used to treat the patient effectively and safely. The present invention has several advantages over the standard method of monitoring the conductivity or the pH of the dialysate to ensure the correct proportion of the bicarbonate and acid concentrates. One advantage is that the need for calibrating the conductivity monitor or pH monitor can be eliminated. Another advantage is that this invention allows a user who does not possess advanced technical training to obtain a quick and reliable visual confirmation of whether the bicarbonate and acid concentrates are present in the correct proportion in the dialysate. Finally, the tests of this invention are easy to use and interpret.

[0073] Although several broad examples which incorporate the present invention have been described above, it is to be understood that the present invention is not to be limited by the examples disclosed herein. Indeed, the disclosure and examples above teach one of ordinary skill a virtually limitless number of conditions which would be within the scope of the claims appended hereto.

Claims

1. A test strip (10) for confirming a desired proportion of components in dialysate, which comprises a first medium capable of indicating the concentration of bicarbonate ion in the dialysate; and a second medium capable of indicating the concentration of glucose in the dialysate.

2. The test strip of claim 1, wherein the first medium is impregnated within and localized at a first region (11) of the test strip, the second medium is impregnated within and localized at a second region (12) of the test strip, and the first and second regions are slightly separated.

3. The test strip of claim 1 or claim 2, wherein the first medium includes an acid and a chromogenic pH indicator.

4. The test strip of claim 3, wherein the acid has a pKa of 2.9 to 5.6.

5. The test strip of claim 4, wherein the acid is selected from citric acid, succinic acid, tartaric acid, phthalic acid, fumaric acid, and gluconic acid.

6. The test strip of any of claims 3 to 5, wherein the chromogenic pH indicator has a pKa value of 3.8 to 7.6.

7. The test strip of claim 6, wherein the chromogenic pH indicator is selected from bromophenol blue, methyl orange, tetrabromophenol blue, congo red, bromocresol green, litmus, and phenol red.

8. The test strip of any preceding claim, wherein the first medium further includes an inert dye.

9. The test strip of any preceding claim, wherein the second medium includes a glucose oxidase enzyme, a peroxidase enzyme, and a chromogenic oxidation/reduction indicator.

10. The test strip of claim 9, wherein the chromogenic oxidation/reduction indicator is selected from o-dianisidine,

4-AAP/phenol, MBTH/3-dimethylaminobenzoic acid, tetramethyl benzidine, and potassium iodide.

11. The test strip of any preceding claim, wherein the second medium further includes an inert dye.

12. The test strip of any preceding claim, which additionally comprises a third medium capable of indicating the pH of the dialysate.

13. The test strip of claim 12, wherein the third medium is impregnated within and localized at a third region (13) of the test strip.

14. The test strip of claim 12 or claim 13, wherein the third medium includes a pH indicator.

15. The test strip of claim 14, wherein the pH indicator has a pKa value of 6.8 to 7.9.

16. The test strip of claim 14, wherein the pH indicator has a pKa value of 7.0.

17. The test strip of claim 14, wherein the pH indicator is selected from bromothymol blue, pyrocatechol violet, tetrabromophenol sulfonephthalein, neutral red, phenol red, and cresol red.

18. The test strip of any preceding claim, which comprises pads respectively impregnated with the first and second media, and a strip of backing material (19).

19. A method for confirming a desired proportion of components in dialysate, which comprises exposing the test strip of any preceding claim to the dialysate; and inspecting the test strip for indication of the concentration of bicarbonate ion, the concentration of glucose and, if the third medium is present, the pH of the dialysate.

20. The method of claim 19, wherein the concentration of bicarbonate ion in the dialysate is 0 to 1655 mEq/L.

21. The method of claim 19, wherein the concentration of bicarbonate ion in the dialysate is 21 to 50 mEq/L.

22. The method of claim 19, wherein the concentration of bicarbonate ion in the dialysate is 35 to 39 mEq/L.

23. The method of any of claims 19 to 22, wherein the concentration of glucose in the dialysate is 0 to 90 g/L.

24. The method of claim 23, wherein the concentration of glucose in the dialysate is 1.55 to 2.57 g/L.

25. The method of claim 23, wherein the concentration of glucose in the dialysate is about 2.0 g/L.

26. The method of any of claims 19 to 25, wherein the pH of the dialysate is 6 to 8.

27. The method of claim 26, wherein the pH of the dialysate is about 7.0.

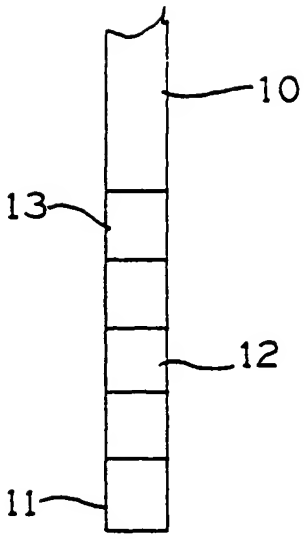

FIG. 1

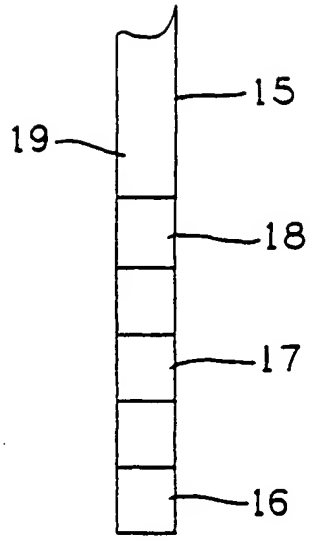

FIG. 3

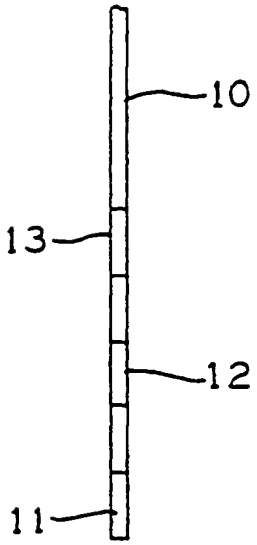

FIG. 2

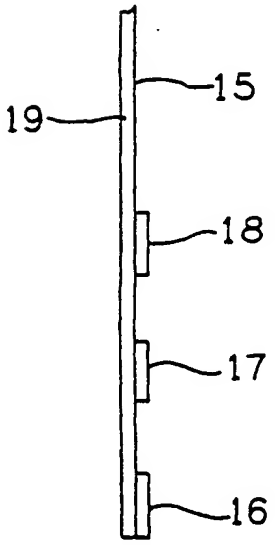

FIG. 4